THE REPAIR OF BONE, WITH SPECIAL REFERENCE TO TRANSPLANTATION AND OTHER ARTIFICIAL AIDS. By A. N. M'Gregor, M.D., Glasgow.[1] (Plate IV.)

The subject of this article is of importance both to the anatomist and to the surgeon: to the former, because the minute anatomy of the processes of repair, and the origin of these processes, are still regarded as uncertain; and to the latter, because an intimate knowledge of the means which Nature employs in the repair of bone lesions is necessary to one whose endeavour is to facilitate recovery. This twofold interest has stimulated researches which have elicited most important discoveries, particularly as to the vitality of bone and of periosteum. We now know that these structures are capable of living after transplantation, and that they exercise the function of bone production in their new position.

Surgeons have made use of this information, and have transplanted bone to repair lesions where the natural processes have failed. There are, however, some points of doubt as to the behaviour of the transplant and its value as a bone producer.

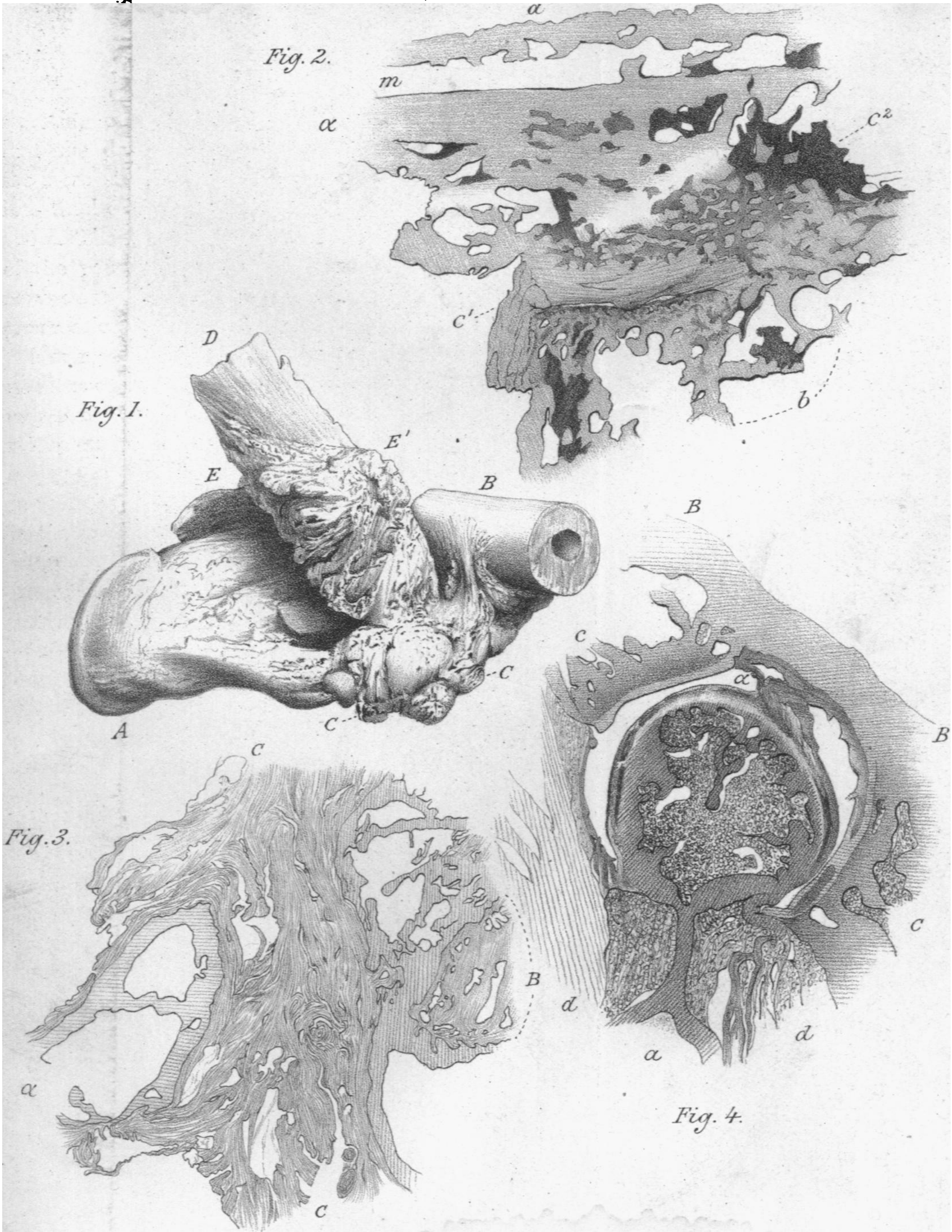
With the object of adding to our knowledge of the subject, particularly with regard to the above-mentioned points, the author performed a number of experiments, the details of which and the results are embodied in this paper.[2]

The most interesting features of a pathological museum are the new formations and results of reparative processes which have arisen to restore the functions of diseased parts. In lesions of the osseous system these changes are very remarkable for their frequency and extent.

Professor Buchanan's Museum in the Western Infirmary of Glasgow contains a unique specimen of compound double fracture of the femur [No. I. C. 12], which illustrates in a remarkable

[1] This paper is the substance of a thesis presented to the University of Glasgow for the degree of M.D., and which received commendation.

[2] The experiments were made while the author was resident in France.



REPAIR OF BONE.

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way the vitality and productive power of periosteum. Figure 1 is a drawing of the specimen.

The bone is broken in two places. The middle piece, *d*, lies between, and transversely to, the lower and upper ends of the upper and lower fragments. This displaced portion is completely necrosed, but new bone has been formed in considerable quantity, and so distributed as to form a sheath round the necrosed part, E^1, E^2, and a strong band of union between the upper and lower fragments in such a way that the function of rigidity is restored. The lower third of the shaft, *A*, is separated from the upper fragment, *B*, by the middle (necrosed) portion and its sheath of new bone, but attached to it by a column, *C*, *C*, of new bone, evidently produced from the upper end of the lower fragment where the column is almost directly continuous in its long axis, and is thicker than at its upper attachment. The junction of this new bone to the upper fragment takes place on the inner side of the latter about 2 inches from its lower extremity. The bony sheath of the dead portion is attached to the anterior surface of this column, and also to the lower end of the upper fragment. This mass of new-formed bone joins the upper and lower fragments, so that the repaired femur is perfectly rigid.

The patient had fallen from the rigging of a ship on to the deck, and, there being no surgeon on board, he was placed in his hammock without any attempt being made at fixation of the limb or treatment of the wound. When, after some weeks, the ship came into port it was found that the necrosed portion projected through a suppurating wound.

The experiments of Dr Macewen[1] have shown that "isolated fragments of bone can live even after transplantation;" and it seems fair to suppose that the fragment in this case would have lived but for the septic condition of the wound. The most interesting feature, however, is that, notwithstanding the presence of conditions so adverse to the repair of tissue, this extensive new formation has resulted. The existence of that bone prompts a query as to its origin.

Dupuytren held that the periosteum alone, through the medium of callus—distinguished as provisional and permanent

[1] Macewen, *Annals of Surgery*, 1887, vol. vi.

—was to be credited with the power of producing bone; again, Wagner asserted that from the diploë, as well as from the periosteum, callus was formed, which became ossified, and repaired the breach of continuity between two fragments of a broken bone. Paget, Virchow, Cornil, and Billroth have declared that new bone is formed from various substances, such as extravasated blood, serum, medullary tissue, &c.

In the case in point the disposition of the new bone round the detached fragment would seem to demonstrate that the vitality of the periosteum had not been destroyed, but that it had lived and enclosed the original bone with a sheath of new bone. It is scarcely possible that the periosteum could have produced the column of bone which unites the upper and lower fragments, for the new formation does not extend to the inner edge of the upper end of the lower fragment, and between the two edges can be seen absorption spaces in the old bone. From its position over the medulla and outer half of the broken surface, it is more likely that the new growth was due to the activity of the medulla, periosteum of the outer edge, and perhaps the hard bone itself.

The specimen shows grounds for the comparison of the vitality of the different parts. They were in the same wound; the detached portion of bone is necrosed, but its periosteum has lived and given rise to new bone, while the fragments which retained their vascular connections have manifested a greater amount of reproductive activity. The inference seems to be that bone deprived of its vascular supply has less vitality than periosteum under the same circumstances. Thus it would seem that periosteum is the most potent factor in bone production, since its vitality is greater than that of the medulla and hard parts.

Turning now to the records of experimental work, we have, on the authority of Macewen, that "not only do detached portions of bone deprived of their periosteum live when reimplanted in their position, but such portions are capable of living after transplantation. Parts of the deeper layers of bone without periosteal connection have been transplanted and lived and grown." It is not stated whether the transplant employed to fill up an abnormal cavity takes any active part in the cementing of itself to the pre-existing bone on which it is planted. There are experiments published to show that it does take an active part in the repair of the breach, but the results are open to question. Nussbaum[1] relates a case of fracture of the ulna in which ligamentous union had taken place; the radius was intact. He cut down on the seat of fracture and removed the ligamentous portion; then he removed a piece of the shaft, at the fractured end, 2 inches long and to half its thickness, and inserted it between the ends of the fragments. The wound healed well, and the ulna became rigid. Now, it is not shown whether the remaining gap was filled up from the transplant or from the rawed surfaces of the original fragments, though the transplant is supposed to have been the active agent.

Macewen[2] published a case in which he transplanted chips of tibia, got from a case where he performed osteotomy for genu valgum, in place of a humerus lost by necrosis. He cut down to where the periosteum was supposed to be and inserted the chips of bone, with the result that a considerable quantity of new bone was produced. Here, too, the question as to the exact origin of the new bone is not definitely solved, though it is assumed that the transplants were the authors. It was not suggested, though it is possible, that the periosteum survived the death of the bone, and the transplants being inserted in its vicinity may have roused its latent power of bone production. The great vitality of the periosteum is illustrated in the first case cited, and is not a rare thing to see necroses of the whole shafts of bones encased in new bone which could only arise from the periosteum.

Trueheart[3] records a case in which he grafted pieces of periosteum to restore the middle third of a clavicle which had been shot away. Fresh transplants were inserted three times a month for two months, when 2¾ inches of bone had been produced. The periosteum was from a newly-killed dog. This example testifies to the remarkable vitality of periosteum, for it lived and produced bone after transplantation into an animal of a different species.

Dr Moore[4] gave the history of a case in which he believed that an inch of new bone was produced from the medulla alone. He reduced an old dislocation of the hip, the head of the femur being on the dorsum ilii, by section of the surgical neck and continued extension. Bony union took place. Subsequently he found at the *post-mortem* examination that new bone had been formed between the shaft and the head of the bone to the extent of 1 inch. He excludes periosteal aid, because that structure could not have stretched, and therefore gives out as his opinion that the new formation was attributable to the medulla. It seems equally reasonable to argue that in simple fractures the medulla alone repairs the mischief, the only difference being that there is a greater amount of intermediary callus in the former case.

Taking advantage of the osteogenic property of periosteum,

[1] *Medical Times and Gazette*, 1875, vol. i. p. 44.

[2] *Lancet*, 1881, vol. i. p. 875.

[3] *Medical Press and Record*, 1885, Oct. 21, p. 382.

[4] *Lancet*, July 1, 1882, p. 108.

Schüller[1] artificially increases the growth of bone by producing a chronic inflammatory process of moderate intensity. His methods are:—" 1. Production of a passive hyperæmia of the part by means of a constricting elastic band round the limb. 2. By placing the patient in such a favourable position as will best facilitate bone growth. 3. Constitutional treatment. 4. By local operations, such as the insertion of steel pins." Following on the same lines, Mickuliez[2] employed them successfully in cases of pseudarthrosis. He cut through the soft parts and periosteum, and inserted turpentine dressings under the latter. The dressings were renewed every three days. Ollier, with the same object, employed the method of driving in lead nails.

Seydel,[3] in a case of fracture of the parietal bone, filled up the gap with chips of tibiæ, the periosteum being retained.

The above quotations show that bone still in possession of its vascular supply is capable of very extensive new formation, that this power is present to a high degree in the periosteum—perhaps on account of its greater vascularity—and to a much lower degree in the medulla and hard parts. The question as to the mode in which the transplant acts has exercised the minds of scientists; Dr Macewen submits two propositions:—(1) That the soft parts of the transplanted bone live, and the hard parts become incorporated with the new-formed bone; and (2) that the transplant acts only as a provisional prop, which is ultimately softened, absorbed, and got rid of by excretion.

There is another way in which the transplant may act, and this explanation is based on the results of the experiments about to be narrated, viz., that the transplant retains its original composition, takes little active part in the production of bone, and exists passively, fixed by the newly-formed osseous tissue which is mainly the product of the original bone. It is virtually a comparatively non-irritant foreign body—for no foreign body can be absolutely non-irritant—which by its bulk fills up a pre-existing cavity, which has little influence on new formative processes apart from the mechanical irritation of its presence, and which, by its bulk and rigidity, hastens recovery by necessitating a less amount of new formation.

In presenting details of the experiments it should be remarked that every case is put down irrespective of the result. The causes of failure are apparent, and may here be prefaced:—In the first place, those numbered I., II., III., VI., and VIII. were attempts

[1] *Berliner Klinische Wochenschrift*, Jan. 14, 1890.
[2] *Medical News*, July 6, 1890.
[3] *Centralblatt für Chirurgie*, March 23, 1890.

to substitute bone, degelatinised by boiling, for the piece of bone excised. They were all unsuccessful. It was with the object of discovering whether the calcareous framework of bone would be utilised by the organism in the production of new bone either by absorption and re-deposition or by the filling of the interstices with callus and bone corpuscles. The failures may not prove that the impossible was attempted, but a comparison with the results of the transplantation of living bone shows the latter to be more practicable. While these experiments were in progress the *Medical News*[1] published the results of Hopkins' experiments, in which he found that sterilised bone, placed in contact with living bone under favourable conditions, becomes absorbed, and when placed in contact with the periosteum undergoes organisation. The other failures were due to the difficulty of administering chloroform to rabbits, and of applying suitable apparatus to insure rigidity of the limb.

Experiment I.—On March 27, 1890, a rabbit was chloroformed, the fur of its left hind leg removed, and the skin well washed with carbolic solution (1 : 20). An incision was made over the tibia, and 1 inch of its shaft removed, and replaced by a similar piece of bone which had been boiled for eight hours, and then kept for twelve hours in corrosive sublimate solution (1 : 1000) till operation time, when it was warmed in a 1 : 2000 solution. Salol dressings and lateral splints were applied.

April 1.—The animal died to-day. Since the operation it has grown much thinner. The dressing contained a small quantity of serous discharge; the skin wound was closed, and no trace of suppuration found. The foreign bone was in good position, surrounded by a sheath of fibrinous matter. On gently separating it a quantity of plastic material was found projecting from the original bone to the medulla of the foreign bone; it had a fibrous appearance, and was pink in colour. No pus was seen.

Experiment II.—On April 2 a rabbit was put under the influence of chloroform and the previous operation repeated, the only difference being that the bone had been boiled for fifteen hours.

April 9.—To-day the dressings were undone, and found to contain a little blood and serous fluid. The position was good, and primary union of the skin had taken place. No sign of suppuration.

April 14.—To-day the rabbit died. The foreign bone had so altered in position as to lie at right angles to the original bone. Suppuration had taken place; the pus was thick, and of a creamy colour, it had no smell, nor had it found exit. The skin wound had closed.

[1] *Medical News*, July 13, 1890.

Experiment III.—April 9.—To-day a rabbit was chloroformed, and after the usual preparations received, in place of $\frac{3}{4}$ of an inch of its tibia, a similar sized piece of bone, which had been boiled twenty-one hours. Dressings and splints were applied.

April 19.—Dressings were undone to-day; the wound is healed, and the bone is in good position.

April 26.—The dressings, on being removed, disclosed the end of the foreign bone projecting through the skin, which had sloughed; it was lying loose in a small quantity of pus, and was extracted without difficulty. Dressings were reapplied.

May 9.—The wound is healed, and the rabbit is well.

Experiment IV.—April 9.—To-day a second rabbit was anæsthetised, and, after the usual preparations, an incision was made over the tibia, and $\frac{3}{4}$ of an inch of the tibia removed. In its place the piece removed from the preceding rabbit was inserted, the transplant having, in the interval, lain in a warm 1 : 2000 solution of hyd. bichlor. The wound was sutured, and salol dressings applied.

April 19.—To-day the dressings were undone, and found to contain a quantity of serous discharge from the lower corner of the wound, where a stitch had cut through the skin. The wound appeared to be aseptic, and the transplant in good position.

April 24.—On removing the dressings to-day it was found that the skin had sloughed, owing to the altered position of the transplant, which was lying loose. It was removed and the wound dressed.

Experiment V.—The first rabbit to have been operated on to-day died under chloroform; a piece of its tibia was excised and kept warm in a solution of hyd. perchlor. (1 : 2000). The bone had been stripped of its periosteum.

The second rabbit received this fragment in place of the middle third of its humerus twenty minutes after excision. The usual dressings were applied.

June 7.—The dressings were undone to-day. The wound was whole, but the transplant was slightly changed in position, so that its upper end was internal to the lower extremity of the upper fragment of original bone.

June 11.—The dressings were again undone, and it was not thought necessary to renew them. The transplant was firmly fixed, and no sign of inflammatory mischief was apparent. The animal freely used the leg.

August 10.—The rabbit was killed to-day, and its humerus with the transplant were put in a decalcifying solution.

Experiment VI.—June 11.—To-day the left radius of a rabbit was laid bare, and a piece of the shaft, about 1 inch in length, was removed and put into a warm (1 : 2000) solution of corrosive sublimate. In its place a piece of bone, which had been boiled for twenty-one hours and warmed in the above solution, was inserted. In this case the muscles were stitched together by deep sutures, so as the better to secure the foreign bone.

June 19.—To-day the wound was found quite healed up, the limb seemed fairly rigid, and the animal was in good condition. The cicatrix was covered with collodion and the splints reapplied.

June 23.—A slight swelling has appeared at the upper end of the incision, and on pressure a few drops of thick creamy pus exuded. The leg was washed with carbolic lotion (1 : 20) and dressings applied.

June 30.—The foreign bone came away through the hole caused by sloughing of the soft parts.

Experiment VII.—June 11.—This operation consisted in replacing the middle third of a rabbit's humerus by the piece of bone excised from the rabbit previously operated on. The bone transplanted had been about half an hour in the warm antiseptic solution.

June 19.—The dressings were removed to-day for the first time. The wound was healed, and it was not thought necessary to renew the dressings. The splints were reapplied.

June 30.—This rabbit is well; bony union has taken place, though not without a considerable amount of deformity.

September 10.—The rabbit was killed to-day, the bone and transplant were excised and put into a decalcifying solution.

Experiment VIII.—To-day a rabbit had a piece of degelatinised bone inserted in place of part of the shaft of its radius. The usual precautions were taken, and salol dressings applied.

July 8.—The dressing became loose four days ago, the bandage being gnawed through by the rabbit. The bandage was reapplied too tightly, and the limb became gangrenous.

Experiment IX.—The living bone from the previous experiment, after lying in a warm 1 : 2000 solution of hyd. bichlor. for twenty minutes, was transplanted among the deep muscles of the back of this rabbit—sine periosteum. The usual precautions were taken to procure asepsy.

July 8.—The skin is tense, and shows signs of sloughing. A stitch was loosened, but no pus exuded.

July 20.—The skin has sloughed, and the transplant is lying in the dressing. (In this case the transplant seems to have been too large.)

Experiment X.—August 7.—This rabbit had about an inch of its left radius replaced by a piece of similar size from the rabbit of the next experiment, both being under chloroform at the same time. Salol dressings and the usual apparatus were applied.

August 14.—Great difficulty has been experienced with this rabbit, it has undone the dressing twice by gnawing through the bandages during the night. Suppuration has ensued, and failure is the inevitable result.

Experiment XI.—This operation consisted in the exchange of about an inch of the shaft of the radius for a like piece of the previous rabbit.

August 14.—As in the previous case, this rabbit has acquired the knack of biting through its bandages, necessitating a renewal of the dressings twice since the operation. In this case, however, sepsis has not occurred.

August 20.—To-day the leg was dressed, and the transplant was found displaced, so that one end projected through the skin. An attempt at withdrawal showed how firmly it was fixed. Dressings were renewed.

September 13.—The animal was chloroformed, and an attempt made to cut off the projecting piece of transplant. The bone splintered, and spoiled the result.

Experiment XII.—October 29.—This rabbit had a portion of its humerus excised, the periosteum being left and the wound in it stitched. The animal died shortly after the operation.

Experiment XIII.—October 29.—This rabbit had a portion of its humerus excised with the periosteum, and the bone from the previous one was inserted.

October 30.—The rabbit undid the bandage, and another one was applied.

November 10.—The dressings were renewed. The wound is whole, and the position of the transplant is fairly good.

November 20.—The dressings were taken off. Bony union has taken place, the transplant being in fair position.

January 28.—The rabbit was killed to-day, and the bone put into a decalcifying solution.

The figures in Plate IV. illustrate various stages of the process.

The specimen from Experiment V. showed that the transplant had been united to the upper fragment end to end, and almost in the same plane, but to the lower fragment at an open angle. Figure 2 is a drawing of the microscopic section at the junction of the transplant and upper fragment. The transplant (a, a) for the most part retains its normal structure, but at the upper end it contains a number of absorption spaces of various sizes, the largest being at the end of the transplant. In none of the lacunæ is there evidence of new formation. The end of the original bone (b) is seen to be greatly excavated, and presents evidence of considerable new formation in the spaces and in the area between it and the transplant. Between C^1 and C^2 there are numerous spaces in the new bone which are connected in some places, and which are directly continuous with the original bone. This network of spaces is greater towards C^2, and the connection with the old bone is more patent than at C^1, where there is a layer of fibrous tissue separating the old bone from the new, on the transplant side of which there is an area of granular fibrous tissue in process of ossification. The bone transplanted was stripped of its periosteum, and though it has lived there is little evidence of reproductive activity, and the new bone uniting it to the original bone seems to be almost entirely the product of the latter.

The specimen from Experiment VI. showed that the transplant in this case had changed position, so that the upper end of the transplant is not quite in the same plane as the upper fragment of original bone. Drawing 3 represents the transplant, *a*, attached to the original bone, *b*, by a mass of connective tissue, *c,c*, composed of new bone, cartilage, and fibrous tissue. The new bone is in greatest quantity near the original bone, and the fibrous tissue is most abundant round the end of the transplant, but these tissues are very irregular in disposition. The transplant contains very few absorption spaces; but the original bone is greatly excavated, and some of the lacunæ are in direct communication with the new bone. The main part of the transplant is unchanged in structure, and shows almost no reproductive activity.

Figure 4, from Experiment XIII.—This experiment has resulted in the fixation of the transplant to the original bone a little above the lower extremity of the latter, primarily by means of a false joint. The rounded end of the transplant is covered by a layer of cartilage, *a*, and fits into a socket, the sides of which are composed of new bone, *c*, also lined with cartilage. This new bone is distinctly seen to be the product of the original bone, and the fibrous tissue joining it to the transplant is granular, and contains large cells, evidently becoming ossified. The head of the transplant is greatly excavated, and the staining with logwood shows that fresh depositions of bone are taking place in the spaces. At that point where the end of the transplant, *a*, is nearest the original bone, *b*, the two are joined together by fibrous tissue containing large cells, and being of a dark granular appearance. The transplant here has undergone considerable change of structure at its upper end, and reproduction is apparent in the fresh depositions of bone in its spaces; but the original bone has been much more active, since it has produced sufficient bone to encircle the end of the transplant. The ossification of the fibrous tissue, *d*, between the transplant and the new bone forming the joint was so far advanced as to make the union rigid. No synovial membrane was discovered in the joint.

The specimen demonstrates the great productive activity of the original bone which has so enclosed the foreign bone, whose new formations have taken place mostly within itself.

The results of the microscopic examination of these three specimens bear out the statement made above, that the transplant takes little part in the production of the bone which unites it to the original bone. They show that the transplant for the most part retains its original composition, and lives.

The sections show the changes which have occurred three months after the bone was transplanted, and seem to prove that the transplants do not undergo absorption of their hard parts so as to completely alter this structure.

Besides assisting in the solution of the question as to the ultimate end of the transplant, these results may be taken as supporting the operation of transplantation of living bone in preference to insertion of decalcified bone, ivory, and other substances which become absorbed. They seem to show that the vitality of the transplant is sufficient to dispense with the method of transplanting one end of the bone, and keeping the animal in a painfully disagreeable position till union takes place before the operation is complėted.

It is possible that when the transplant acquires a better vascular connection it may take a share in the production of bone, and it would be interesting to know the condition of the transplant six months or a year after the operation. There are other questions of interest, such as the liability to fracture, the repair of such a fracture, and the behaviour of the transplant when the patient becomes affected by such constitutional diseases, as sometimes cause degeneration and softening of the union of simple fractures.